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Management and diagnosis of tuberculosis in solid organ transplant candidates and recipients: Expert survey and updated review☆,☆☆

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ABSTRACT

Background: Optimal screening and management of latent tuberculosis infection (LTBI) and active tuberculosis (TB) in solid organ transplant (SOT) candidates and recipients is necessary to prevent morbidity and mortality.

Methods: We conducted a cross-sectional survey of TB and transplant experts across the United States reviewing the clinical practice preferences on key management issues related to LTBI and TB in SOT candidates and recipients.

Results: Thirty TB and 13 SOT experts were surveyed (response rate = 53.8%). Both groups agreed that tuberculin skin test (TST) and chest x-ray screening in SOT candidates was useful (78.6% and 84.6%, respectively). TST after SOT was not useful for most transplant experts and TB experts (0% vs. 32.1%, respectively), but both groups were split on usefulness of interferon gamma release assays (IGRA) in SOT recipients (42.9% TB experts vs. 46.2% SOT experts). Most experts recommend LTBI treatment prior to SOT if close monitoring is assured (82.1% TB experts vs. 76.9% transplant experts). LTBI treatment with isoniazid was preferred for patients on calcineurin inhibitors. Evaluation for suspected TB in SOT recipients varied, but most TB experts favored sputum testing (88.9%) whereas most transplant experts favored bronchoscopic testing (69.2%). Preferred TB treatment regimens in SOT recipients were similar to regimens recommended for immunocompetent patients.

Conclusions: Most TB and transplant experts recommend evaluation and treatment for LTBI in SOT candidates. Liver transplant candidates, however, should only be treated if close monitoring can be assured and after consulting with a hepatologist. Practice preferences varied regarding the initial diagnostic approach for suspected TB in SOT recipients; however, most experts agreed that SOT recipients should receive similar treatments as immunocompetent patients.

Introduction

Tuberculosis (TB) incidence in solid organ transplant (SOT) recipients is reported between 0.25 to 13.7%, and occurs more often in countries and settings with high prevalence of TB [1–5]. Moreover, TB in SOT recipients carries high TB-related and SOT-related morbidity and mortality. The most recent TB consensus guidelines in the United States addressed the diagnosis in immunosuppressed individuals and some aspects of TB treatment in SOT recipients, such as drug-to-drug interactions with anti-TB medications. They do not, however, provide a dedicated section with recommendations for the diagnosis and management of LTBI and TB in various types of SOT candidates and recipients [6–9]. The Spanish Society of Infectious Diseases and Clinical Microbiology previously put together a consensus statement to provide

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clinical guidelines specifically for the management of SOT recipients in 2009 [10]. Several of those recommendations are based on expert opinion and retrospective data [11]. However, it is unclear if consensus between TB and SOT experts exists, if there are TB management practice variations between Spain and the US, and some key clinical issues remain unaddressed.

Important considerations in SOT candidates are clinical evaluation of latent tuberculosis infection (LTBI) with the tuberculin skin testing (TST) and/or interferon gamma release assays (IGRAs), the utility of routine screening chest x-rays (CXR), and LTBI treatment regimens (especially in liver transplant candidates). In SOT recipients, important considerations are diagnostic accuracy of testing for LTBI, diagnostic approach for suspected active TB, and treatment regimens for LTBI and active TB.

Anti-TB medications, specifically rifamycins (rifampicin, rifabutin, or rifapentine) interact with calcineurin inhibitors (i.e. cyclosporine and tacrolimus), mammalian target of rapamycin (mTOR) inhibitors (i.e. sirolimus and everolimus), and corticosteroids by reducing serum levels of these medications potentially precipitating graft rejection and dysfunction [6,12,13]. For these reasons, the use of rifamycin-based regimens for the treatment of LTBI and active TB in SOT recipients is controversial [14]. Moreover, common LTBI regimens have associated risk of hepatotoxicity. Isoniazid and rifamycins can cause drug-induced hepatitis, and the previously used combination of rifampicin/pyrazinamide can cause severe liver toxicity [6,10]. This raises the issue of how to best treat liver transplant candidates with LTBI or liver transplant recipients with LTBI or active TB.

To help address these key clinical issues, the American College of Chest Physicians (ACCP) sponsored a project to conduct a national survey that invited United States experts in TB and SOT to compare medical preferences for common TB diagnostic and management questions in SOT candidates and recipients. After reviewing the recently released American Thoracic Society(ATS), Centers for Disease Control and Prevention(CDC), and Infectious Disease Society of America(IDSA) diagnostic and treatment guidelines, we decided to publish this original work and discuss our findings in comparison with the most recent published data [7,9].

Material and methods

The study was reviewed and approved by the Mayo Clinic Institutional Review Board and was research exempt.

We conducted a web-based survey amongst TB and transplant experts from August 18, 2009 to June 21, 2010.

Development of survey questionnaire

No validated questionnaire regarding TB practices in SOT existed. Therefore, a seven-member steering committee representing pulmonary and infectious diseases TB experts and transplant experts reviewed the literature and developed potential survey questions utilizing the Delphi method. The survey questions were focused on the following clinical themes: (1) diagnostic utility of TST and IGRAs, before and after SOT, (2) usefulness of routine CXR in assessment of candidates undergoing SOT evaluations, (3) LTBI treatment alternatives for patients taking calcineurin and/or mTOR inhibitors, (4) management of LTBI, before or after liver transplantation, (5) diagnostic work-up and treatment alternatives for active TB after SOT. Responses were formatted on a 5-point Likert scale or for priority ranking, and comments were allowed. The proposed questionnaire and survey instructions were reviewed by non-TB experts and non-transplant experts from the ACCP Chest Infection Network for clarity and comments. The questionnaire was revised accordingly. One question, in which consensus guidelines exists for the treatment of patients with active TB in general, was included for internal validation. The final questionnaire had 11 questions (see Appendix A).

Selection of study participants

We sought a representative sample from the sampling frame of TB and SOT experts of varied institutions and geographic regions from the United States to avoid bias based on regional practice variation and differences in TB prevalence. TB and SOT experts were identified in three ways: (1) nomination by the study's steering committee based on known contributions in the field of TB or SOT; (2) through a PubMed publication search using terms “tuberculosis” and “solid organ transplantation” and/or; (3) practitioner in a TB or SOT referral center in the United States obtained from the ACCP and other professional organizations databases. Inclusion criteria for TB experts included physicians who care for TB patients in a referral practice and/or have published one or more research articles on TB. TB experts were comprised of the following specialties: Pulmonary Medicine, Infectious Diseases, and Internal Medicine. Transplant experts included physicians who manage SOT patients in referral centers and/or published one or more research articles related to SOT. SOT experts were comprised of Pulmonary Medicine and Infectious Diseases specialists. Experts were sorted by their contributions to the respective fields (SOT or TB) and current practice setting, not by specialty training.

Survey procedure

Need for consent was waived by the IRB. The self-administered, web-based questionnaire was sent to participants via an email invitation. The email included survey instructions, voluntary nature of the study, a statement regarding the purpose of the study, identification of the study sponsor and principal investigator, and an option to accept or decline participation as previously described [14]. If no response was received within 2 weeks, a subsequent e-mail invitation was sent. If there was no response by four weeks, the e-mail address was reconfirmed and a follow-up invitation was sent at 6 weeks and if necessary 8 weeks. On failure to obtain response after the fourth invitation, experts were deemed non-participators. No incentive or remuneration was offered.

Measurable outcomes

The measurable outcomes were level of agreement amongst experts and order of preference on priority ranking.

Definitions

Agreement was defined as responding either “agree” or “strongly agree”, and disagreement was defined as responding “disagree” or “strongly disagree”. Neutral responses were counted in the denominator. Consensus level was defined when 80% of respondents in a category were in agreement or disagreement.

Table 1
Comparison between TB and transplant experts for LTBI diagnosis and management questions surrounding solid organ transplantation.

Question	TB experts % agreement (N = 29)	Transplant experts % agreement (N = 13)	*p*-value
TST prior to SOT	78.6% (N = 28)	84.6% (N = 13)	1.0
TST after SOT	32.1% (N = 28)	0% (N = 13)	0.038*
CXR prior to SOT	76.9% (N = 26)	69.2% (N = 13)	0.704
IGRA after SOT	42.9% (N = 28)	46.2% (N = 13)	1.0
LTBI therapy before liver transplantation	78.6% (N = 28)	76.9% (N = 13)	1.0
LTBI therapy after liver transplantation	55.2% (N = 29)	53.9% (N = 13)	1.0

TB = mycobacterium tuberculosis; SOT = solid organ transplant; TST = Tuberculin skin test; CXR = Chest radiograph; IGRA = interferon gamma release assay; LTBI: Latent TB infection; % agreement includes agree and strongly agree answers to questionnaire. Comparison by Fisher's Exact test. (*) $p \leq 0.05$ is considered statistically significant.

Data management

We used the web-based Survey Monkey™ platform to gather and compile the information from the invited experts as previously described [14]. Individual information was confidentially maintained on a password secured folder on a password secured network, and the responses were deidentified.

Statistical analysis

Responses were calculated as percent agreement with each expert group. Categorical data were calculated as percent frequency of occurrence. The Fisher Exact test was used to compare responses between the two groups—SOT and TB experts. A *P* value of <0.05 was considered significant. All statistical analysis was performed using JMP®, Version JMP Pro 10. (SAS Institute Inc., Cary, NC, 1989–2007).

Results

Survey response

Fifty-eight TB experts and 22 SOT experts were identified as potential participants. The overall survey response rate was 53.8% with 43 out of 80 experts responding. This included 13 SOT experts out of 22 (59.1%) and 30 TB experts out of 58 (51.7%) who received the survey. Geographic areas of primary practice for TB experts included the following states: Arkansas, California, Colorado, Florida, Georgia, Illinois, Maryland, Massachusetts, Minnesota, New York, North Carolina, Tennessee, Texas, Virginia, and Washington. Areas of primary practice for SOT experts included California, Illinois, Michigan, Minnesota, New York, Ohio, Oklahoma, and Texas.

Utility of TST for LTBI screening, before and after SOT in average risk patients

Most TB experts and SOT experts (consensus level) agreed that TST was a useful screening tool before SOT (78.6% and 84.6% agreement, respectively; $p = 1.0$) (Table 1). Following SOT, however, some TB experts but none of the SOT experts indicated that TST was a useful screening tool (32.1% vs 0% agreement in transplant experts; p = 0.038).

Routine CXR in the assessment of patients prior to SOT in average risk patients

The majority of TB experts and SOT experts agreed with CXR for evaluation of SOT candidates, 76.9% and 69.2% agreement, respectively ($p = 0.70$) (Table 1). Neither group, however, reached consensus.

Diagnostic value of IGRA for LTBI after SOT in patients with risk factors for TB

No consensus was reached by either group on whether IGRAs represent a useful diagnostic test for LTBI in SOT recipients who had risk factors for TB (42.9% TB experts and 46.2% SOT experts, $p = 1.0$). However, IGRA diagnostic utility was felt to be higher in comparison to TST in this patient population (Table 1).

Treatment of LTBI in liver transplant candidates and recipients

The majority of TB experts (78.6%) and SOT experts (76.9%) agreed in the utility of treating LTBI prior to liver transplantation in patients with end-stage liver disease ($p = 1.0$), provided that close monitoring is assured for those patients (Table 1). Likewise, the majority of TB experts (55.2%) and SOT experts (53.9%) agreed that LTBI should be treated following liver transplantation ($p = 1.0$).

Treatment regimens for LTBI in patients receiving calcineurin inhibitors

TB experts and SOT experts ranked a regimen of daily isoniazid (INH) for 9 months as the first choice for treatment of LTBI in SOT recipients on calcineurin inhibitors (Consensus level: 96.4% and 83.3%, respectively, p = 0.209). The second most common treatment regimen chosen was INH for 6 months (TB experts = 41.4%, transplant experts = 58.3%, p = 0.493). No other single regimen was preferred over another by either expert group.

Diagnostic workup for possible pulmonary TB in patient with cough, fever, and non-cavitary lung infiltrates after SOT

TB experts agreed (consensus level) that the first priority in working up SOT recipients with suspected TB was sputum acid fast bacillus (AFB) smear and culture (82.8%), followed by sputum nucleic acid

amplification testing (NAA) (44.8%). However, the majority of SOT experts chose diagnostic bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsies (TBBx) (69.3%) as first priority with 30.7% choosing sputum NAA and AFB smear/ culture as either second or third priority. Beyond those priorities, no other diagnostic testing was preferred by SOT experts.

Treatment regimens for non-cavitary pulmonary TB with negative sputum culture at 2 months of treatment in SOT recipients

Intensive phase with daily RIPE therapy (i.e. rifampin or rifabutin), isoniazid, pyrazinamide, ethambutol) followed by 4 months of continuation therapy with daily INH and rifampin or rifabutin were the preferred treatment regimens by both TB (55.1%) and SOT experts (76.9%). In addition, some TB experts (20.9%) and SOT experts (15.4%) preferred the same daily antimicrobial treatments options but with a 7 months of continuation phase.

Treatment regimens for cavitary TB with positive culture at 2 months of treatment in SOT recipients

Intense phase with daily RIPE therapy (with rifampin or rifabutin), followed by 7 months of continuation therapy with daily INH and rifampin or rifabutin were the preferred treatment regimens by TB experts in patients with cavitary TB. Over 80% of TB experts chose this regimen as their first or second choice. All SOT experts chose RIPE therapy with daily INH and rifabutin for 7 months as their first or second preference.

Discussion

TB is a serious infection in SOT recipients, which can lead to significant morbidity and mortality [1,5,13,15]. SOT candidates with unrecognized LTBI can also develop atypical and disseminated forms of TB due to chronic illness and/or exposure to immunosuppressing medications. These severe and sometimes difficult-to-diagnose forms of TB are associated with poor outcomes [1,5,13,15]. Thus, TB diagnosis and management in this patient population can be challenging leading to significant practice variation. Survey methodology of current practices can assist to show areas of disagreement and areas of agreement enough to potentially reduce practice variation. This information can be important for practice standardization.

In this context, the most recent international guidelines for TB in SOT candidates and recipients are from the 2009 consensus document from the Spanish Society of Infectious Diseases and Clinical Microbiology. Despite a recent European experts follow-up review, the current ATS/CDC/IDSA guidelines do not fully standardize surveillance, diagnosis, and treatment strategies in SOT candidates and recipients [7–9,12,13]. Moreover, current recommendations for TB management in SOT candidates and recipients are based mostly on retrospective data and expert opinion. In this context, we utilized data from surveyed TB experts and SOT experts across the United States to not only quantify their medical preferences but also to review critical issues in the diagnosis and management of LTBI and active TB in SOT candidates and recipients.

LTBI screening with TST and IGRA in SOT candidates and recipients

TST was the main diagnostic test for LTBI for almost 100 years. About 10 years ago, IGRAs were introduced and became widely available in clinical practice [19]. TST can be flawed with errors in intradermal administration of tuberculin and variability in interpretation [20]. Anergy to the tuberculin antigen is an additional concern in chronically-ill and immunosuppressed SOT candidates and recipients, which can cause false negative results. False-positive TST can occur with prior vaccination with BCG (Bacillus Calmette–Guérin) or infection with other non-tuberculous mycobacteria such *Mycobacterium avium complex* [21]. IGRA uses more specific *M. tuberculosis* antigens than TST and has been recommended in populations with low or intermediate risk, especially in subjects with prior BCG vaccination [7].

In the current study, both TB and SOT experts were in agreement that TST was a useful test for LTBI screening in SOT candidates but the majority of experts felt a limited diagnostic utility of TST in SOT recipients. This is likely secondary to the belief that SOT recipients will likely develop anergy and false-negative TST results. However, in immunocompromised patients, such as HIV patients with low CD4 counts, IGRAs have not been proven consistently superior to TST [22]. Moreover, indeterminate and false negative results can also occur with IGRAs in immunocompromised patients, and some experts suggest using both TST and IGRA in those individuals to maximize the sensitivity of both tests for LTBI screening purposes in high risk populations [8,22–25]. In fact, both TST and IGRA have a low predictive value for TB reactivation and both tests can also yield negative results in immunosuppressed patients who actually progressed to active TB [22,26]. At the time of the survey, we found no clear consensus among TB and SOT experts regarding the diagnostic utility of IGRA after SOT. However, these preferences could have changed over more recent years with increased familiarity with the strengths and limitations of these immunodiagnostic tests. Moreover, a positive TST and/or IGRA test can be diagnostically useful, but negative results need to be interpreted with caution, in particular if patients have prior exposure to TB and/or have CXR findings suggestive of previously untreated TB [13].

Routine CXR in the assessment of SOT candidates

Radiographic presentation of pulmonary TB can be atypical in immunocompromised individuals [12]. While most SOT candidates are not immunosuppressed from a pharmacologic standpoint, many are relatively immunocompromised secondary to their underlying disease and/or chronic illness (i.e. renal or liver failure). In other immunosuppressed populations, such as those with HIV infection, routine use of CXR to assess for active pulmonary TB is not recommended as the test sensitivity varies [27,28]. In our survey, TB experts reached near consensus level agreement on the utility of routine CXR in patient assessment prior to SOT. The majority of transplant experts also agreed with routine CXR prior to SOT, but at lower level of agreement. In clinical practice, most patients undergoing SOT, in particular lung transplant candidates, have chest imaging performed for a variety of reasons other than evaluating for LTBI and TB.

Treatment of LTBI in liver transplant candidates and recipients

A systematic review in liver and renal transplant recipients suggested that treatment of LTBI reduces the risk of TB reactivation

[16,17]. Diagnostic strategies that accurately detect and treat LTBI in SOT candidates and recipients can prevent subsequent morbidity and mortality associated with TB reactivation [18]. End-stage liver disease patients are at risk for liver decompensation with LTBI treatment or TB treatment. They are also at risk of developing disseminated TB following transplantation, which is likely secondary to immunosuppressing medications required to prevent graft rejection [5]. Treatment of LTBI in patients with end-stage liver disease is challenging secondary to the risk of drug related hepatotoxicity that may have a significant impact on marginally reserved liver function [6]. Despite this potential risk, some studies suggest that these patients can be safely treated for LTBI with INH or rifamycin based regimens prior to transplantation [31,32]. In our survey, both TB and SOT experts reached near consensus level of agreement that liver transplant candidates with LTBI should be treated prior to transplantation provided very close monitoring is ensured. However, neither TB nor SOT experts reached consensus on preference for any treatment regimen, and no hepatologist completed the survey. Rifampin daily for 4 months and INH daily for 9 months were the most frequently preferred regimens. Treatment with INH for at least 6 months significantly decreases the risk of developing active TB, and a very small number of patients need to discontinue this regimen secondary to drug induced hepatitis or acute liver failure [17]. However, a more recent report from Canada found that a significant proportion of liver transplant candidates and recipients do not tolerate standard LTBI therapy [18].

Treatment regimens for LTBI in patients receiving with calcineurin inhibitors

SOT recipients receiving calcineurin inhibitors and other anti-rejection drugs are at risk of reactivation of TB, which can be associated with high mortality and morbidity [33]. In immunocompetent patients, LTBI is treated with one of the following regimens: INH daily for 9 months, rifamycin daily for 4 months, or weekly rifapentin and isoniazid for 3 months [6]. Rifamycins are potent inducer of cytochrome P-450 oxidative enzymes leading to decreased serum concentration of calcineurin inhibitors; however, rifabutin has a lower cytochrome inducer effect [9,34]. This important drug-to-drug interaction can potentially lead to graft-versus-host disease (GVHD) or graft rejection and organ failure [12]. Likely for this reason, both TB and SOT experts reached a consensus on INH daily for 9 months as the preferred treatment regimen in patients with LTBI who are additionally receiving a calcineurin inhibitor. This recommendation is also shared by some European experts [12,13]. However, rifabutin is also an effective therapy for LTBI and usually well-tolerated therapeutic option [29,30]. Moreover, rifabutin can be less hepatotoxic than INH and faster to complete with 4 months of treatment, and thus, with accumulating experience using rifabutin along with calcineurin inhibitors or mTOR inhibitors, practice seems to be changing to more often use of rifabutin as the initial therapeutic choice for LTBI as long as careful evaluation, close drug monitoring, and adjustment of the immunosuppression is assured [14,31].

Management of active TB following SOT

Diagnosis of active TB infection in immunosuppressed patients is challenging secondary to atypical clinical features including extra-pulmonary involvement and presence of concomitant infections. Confirmation of diagnosis by isolating *M. tuberculosis* in liquid or solid cultures is time consuming, but NAA and other rapid molecular tests can detect the organism in hours. NAA diagnostic performance does not depend on the immune status of the patients, but false negative results are possible if the organism is not or rarely present in the sample. In suspected active TB after SOT, TB experts reached consensus that 3 AFB sputum smears with subsequent mycobacterial cultures is the preferred initial diagnostic test approach. Interestingly, SOT experts had consensus agreement on diagnostic bronchoscopy with broncho-alveolar lavage and trans-bronchial biopsy to diagnose active TB in this setting. It is unclear why the two group of experts had a different initial diagnostic approach for suspected TB, but it is possible that transplant experts have a lower threshold for bronchoscopic testing to not only diagnose TB but also detect other opportunistic infections that are often in differential diagnosis.

Moreover, no widely accepted treatment regimen for active TB infection in SOT recipients exists. Our study found no consensus amongst TB and SOT experts for treatment regimens in this population. The initial intensive phase with daily RIPE (with rifampin or rifabutin) followed by a combination of INH and rifamycin or rifabutin daily for 4 months were the preferred regimens by both TB and SOT experts. Given the interactions with calcineurin inhibitors and rifamycins, immunosuppressive drug levels need to be closely monitored and adjusted to prevent organ rejection and dysfunction [17]. The Spanish Society of Infectious Diseases and Clinical Microbiology guidelines favor the use of prolonged anti-TB treatment regimens without rifamycins in SOT with localized and non-severe forms of TB [13]. For cavitary TB in SOT recipients, a daily intensive phase with RIPE(with rifampin or rifabutin) followed by INH and rifabutin or rifabutin monotherapy daily for 7 months were preferred regimens by both TB and SOT experts. Once again, continuous monitoring of immunosuppressive drugs levels for patients on calcinurin inhibitors, mTOR inhibitors, and/or corticosteroids is recommended [12,13].

Strengths and limitations of the study

The study had several strengths, including a careful design and review of the questionnaire by an external steering committee of Pulmonary Medicine and Infectious Disease TB experts from most of the United States' regional TB centers. Questionnaire items were also reviewed for clarity by pulmonary physicians from the ACCP who were not experts in TB or SOT. This study also included a large number of TB and SOT experts from various geographic locations and academic centers in the United States, and we had a high response rate of over 50%. However, the diversity in the types of medical subspecialties represented was low, including lack of hepatologist participation in the survey, but a hepatologist was part of the study data analysis and manuscript writing. Although this survey data was obtained in 2010, there have been very few changes in the management of LTBI and TB in SOT candidates and recipients since that time [7–9,13]. Important areas of regarding TB in SOT candidates and recipients were not addressed by this survey. In the future, researchers should explore attitudes and preferences of SOT practitioners toward reduction in immunosuppression during treatment for active TB. In addition, management issues unique to lung transplant should be queried (e.g. singe versus bilateral transplant), and management issues regarding the treatment of LTBI based on the degree of liver failure as determined by liver failure stratification tools.

Conclusions

TB and SOT experts agree that SOT candidates should have appropriate pre-transplant evaluation for LTBI and active TB with either TST or IGRA along with a CXR. Treatment for LTBI in SOT candidates, even in advanced liver disease, should be considered if very close monitoring can be assured and after consulting with a hepatologist. To avoid important drug-to-drug interactions, patients taking calcineurin inhibitors or mTOR inhibitors should receive INH for LTBI therapy, but rifabutin can be also used with close drug monitoring. No consensus was reached regarding the initial diagnostic evaluation for SOT recipients suspected to have active TB; however, both groups of experts did agree that SOT recipients with TB should be treated with anti-TB treatment regimens commonly used for immunocompetent TB patients.

Author contributions

Concept/design: PE; Data analysis/Interpretation: KMP, CCK, PE; Drafting article: KMP, CCK, SC, PE; Critical Revision of article: KMP, CCK, SC, ML, BTM, MB, DEG, BJS, PE; Approval of article: KMP, CCK, SC, ML, BTM, MB, DEG, BJS, PE; Statistics: PE, CCK; Funding secured by: PE

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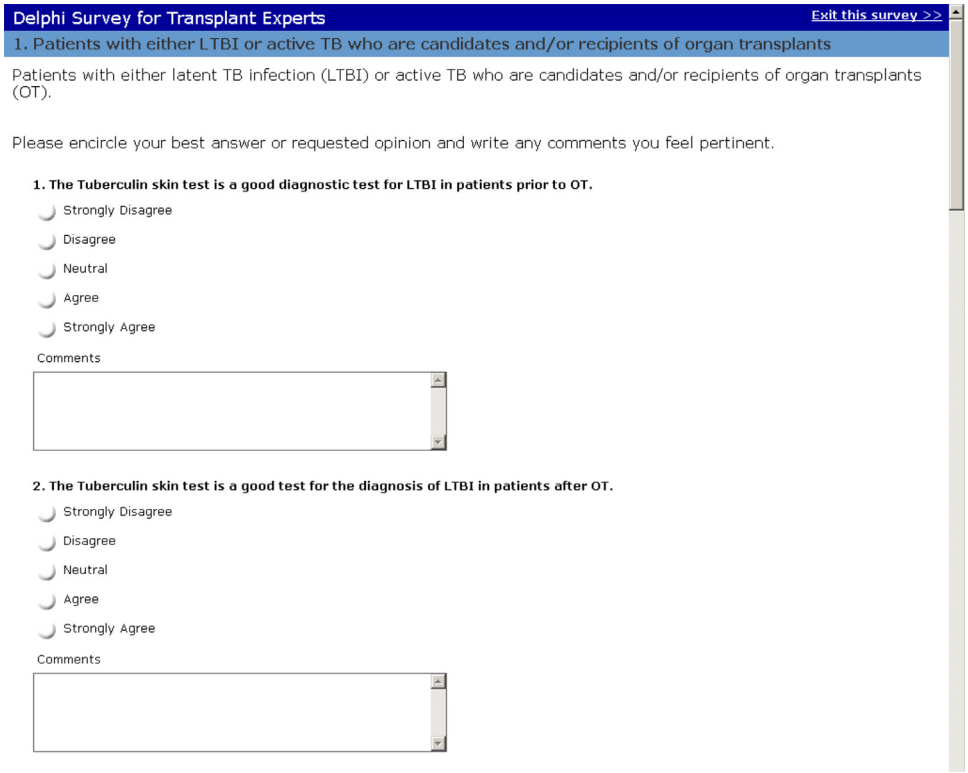
Appendix A


Delphi Survey for Transplant Experts

Exit this survey >>

1. Patients with either LTBI or active TB who are candidates and/or recipients of organ transplants

Patients with either latent TB infection (LTBI) or active TB who are candidates and/or recipients of organ transplants (OT).

Please encircle your best answer or requested opinion and write any comments you feel pertinent.

1. The Tuberculin skin test is a good diagnostic test for LTBI in patients prior to OT.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

2. The Tuberculin skin test is a good test for the diagnosis of LTBI in patients after OT.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

3. The use of skin test controls (e.g. Candida) is of no value in the assessment of OT recipient patients with risk factors for anergy and/or TB infection.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

4. The routine use of chest x-ray is of value in the assessment of patients receiving OT regardless of the TST results.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

5. The use of interferon-gamma release assays (i.e. QuantiFERON TB GOLD and/or T-SPOT.TB) is of value to assess OT recipient patients with risk factors for TB infection.

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

6. Among the following LTBI treatment alternatives, which would you recommend, in order of priority, for all OT patients (on calcinurin inhibitors)?

(1=1st priority to 7= least favored choice; you can skip some of the answer choices)

	1	2	3	4	5	6	7
Isoniazid (INH) daily for 9 months	○	○	○	○	○	○	○
INH daily for 6 months	○	○	○	○	○	○	○
Rifampin (RIF) daily for 4 months	○	○	○	○	○	○	○
RIF + INH daily for 3 months	○	○	○	○	○	○	○
Rifabutin daily for 4 months	○	○	○	○	○	○	○
INH + Rifabutin TIW for 3 months	○	○	○	○	○	○	○
Other treatment	○	○	○	○	○	○	○

If other please specify/comments

7. For the management of LTBI in patients who are candidates for liver transplant; but have end-stage liver disease, would you would treat for LTBI BEFORE liver transplant provided that close patient monitoring is assured:

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

8. For the management of LTBI in patients who are candidates for liver transplant; but have end-stage liver disease, would you would treat for LTBI AFTER liver transplant provided that close patient monitoring is assured:

- Strongly Disagree
- Disagree
- Neutral
- Agree
- Strongly Agree

Comments

9. Among the following LTBI treatment alternatives, which one would you recommend in order of priority for liver transplant candidates or liver transplant patients?

(1=1st priority to 7= least favored choice; you can skip some of the answer choices)

	1	2	3	4	5	6	7
Rifampin (RIF) daily for 4 months							
Isoniazid (INH) daily for 9 months							
INH daily for 6 months							
INH + Rifabutin TIW for 3months							
Other treatment							
RIF + INH daily for 3 months							
Rifabutin daily for 4 months							

If Other please specify/comment

10. In a patient with a history of OT, who presents with a mild non-productive cough, fever, and a chest x-ray showing non-cavitary pulmonary infiltrates; what would you recommend in order of priority as part of the diagnostic work up for active TB?

(1=1st priority to 7= least favored choice; you can skip some of the answer choices)

(BAL= Bronchioalveolar lavage; TBBx= Transbrochial biopsy; interferon-gamma release assay= either QuantiFERON TB GOLD or T-SPOT.TB)

	1	2	3	4	5	6	7
Diagnostic bronchoscopy with BAL+TBBx							
Sputum induction for AFB smear/culture x 1							
Sputum nucleid acid amplification (PCR)							
Diagnostic bronchoscopy with BAL							
Direct surgical lung biopsy							
Sputum AFB smear and culture x 3							
Interferon-gamma release assay							

If others, please specify/comment

11. In a patient with a history of OT, who has been diagnosed with active TB and whose chest x-ray shows non-cavitary pulmonary infiltrates; which TB treatment regimen would you choose in order of priority if the sputum AFB culture is positive at 2 months of treatment?

(1=1st priority to 7= least favored choice; you can skip some of the answer choices)

(*) 4 drugs: Intensive phase with Isoniazid (INH) + Pyrazinamide + Ethambuthol + a rifamycin as recommended by the ATS/CDC/ISDA guidelines.

	1	2	3	4	5	6	7
4 drugs* for first 2 months; INH+RIF daily for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF BIW for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF TIW for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+Rifabutin daily for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF daily for 7 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF TIW for 7 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+Rifabutin daily for 7months	○	○	○	○	○	○	○

If other please specify/comment

12. In a patient with a history of OT, who has been diagnosed with active TB and whose chest x-ray shows cavitary pulmonary infiltrates; which TB treatment regimen would you choose in order of priority if sputum AFB culture is positive at 2 months of treatment?

(1=1st priority to 7= least favored choice; you can skip some of the answer choices)

(*) 4 drugs: Intensive phase with Isoniazid (INH) + Pyrazinamide + Ethambuthol + a rifamycin as recommended by the ATS/CDC/ISDA guidelines.

	1	2	3	4	5	6	7
4 drugs* for first 2 months; INH+RIF daily for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF BIW for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF TIW for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+Rifabutin daily for 4 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF daily for 7 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+RIF TIW for 7 months	○	○	○	○	○	○	○
4 drugs* for first 2 months; INH+Rifabutin daily for 7 months	○	○	○	○	○	○	○

If other please specify/ comment

Done >>

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